

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
7 July 2005 (07.07.2005)

PCT

(10) International Publication Number
WO 2005/060603 A3

(51) International Patent Classification⁷: **C07D 211/38**,
211/46, C07C 233/05

(74) Agent: **GRIEFF, Edward, D.**; Wilmer Cutler Pickering
Hale and Dorr LLP, 1455 Pennsylvania Avenue, N.W.,
Washington, DC 20004 (US).

(21) International Application Number:
PCT/US2004/041069

(81) Designated States (*unless otherwise indicated, for every
kind of national protection available*): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,
ZW.

(22) International Filing Date:
10 December 2004 (10.12.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/528,184 10 December 2003 (10.12.2003) US

(84) Designated States (*unless otherwise indicated, for every
kind of regional protection available*): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,
FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO,
SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN,
GQ, GW, ML, MR, NE, SN, TD, TG).

(71) Applicant (*for all designated States except US*): **NI-
TROMED, INC.** [US/US]; 125 Spring Street, Lexington,
MA 02421 (US).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **GARVEY, David**,
S. [US/US]; 10 Grand Hill Drive, Dover, MA 02030 (US).
XINQIN, Fang [US/US]; 77 Bow Street, Lexington,
MA 02420 (US). **SUBHASH, P., Khanapure** [IN/US];
3 Colonial Drive, Clinton, MA 01510 (US). **RAMANI,
R., Ranatunga** [US/US]; 11 Bates Road, Lexington, MA
02421 (US). **SHIOW-JYI, Wey** [CN/US]; 10 Charnstaffe
Lane, Unit 302, Billerica, MA 01821 (US).

Published:

— with international search report

(88) Date of publication of the international search report:
1 December 2005

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: NITRIC OXIDE RELEASING PYRUVATE COMPOUNDS, COMPOSITIONS AND METHODS OF USE

(57) Abstract: The invention describes novel pyruvate compounds comprising at least one nitric oxide releasing group and pharmaceutically acceptable salts thereof, and novel compositions comprising at least one pyruvate compound comprising at least one nitric oxide releasing group, and, optionally, at least one nitric oxide donor and/or at least one therapeutic agent. The invention also provides novel compositions comprising at least one pyruvate compound and at least one nitric oxide donor compound and/or at least one therapeutic agent. The invention also provides novel kits comprising at least one pyruvate compound, that is optionally substituted with at least one nitric oxide releasing group, and, optionally, at least one nitric oxide donor and/or at least one therapeutic agent. The invention also provides methods for (a) treating cardiovascular diseases; (b) treating renovascular diseases; (c) treating diabetes; (d) treating diseases resulting from oxidative stress; (e) treating endothelial dysfunctions; (f) treating diseases caused by endothelial dysfunctions; (g) treating cirrhosis; (h) treating pre-eclampsia; (j) treating osteoporosis; (k) treating nephropathy; (l) reperfusing injury following ischemia; and/or (m) preserving tissues, organs, organ parts and/or limbs. The nitric oxide releasing group is preferably a nitro group (i.e. NO₂), a nitroso group (i.e. NO) and/or a heterocyclic nitric oxide donor group. The heterocyclic nitric oxide donor group is preferably a furoxan, a sydnonimine, an oxatriazole-5-one and/or an oxatriazole-5-imine.



WO 2005/060603 A3